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TRANSMITTAL OF APPEAL BRIEF (Large Entity)

Docket No. 12.017011 DIV

In Re Application Of: **Soito**

Application No.	Filing Date	Examiner	Customer No.	Group Art Unit	Confirmation No.
10/716,704	11/20/03	Anuradha Roy	38732	3736	7077

Invention: **Cytological Evaluation of Breast Duct Epithelial Cells Retrieved by Ductal Lavage**

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January 6, 2007

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Theodore Allen
Registration No, 41578
Cytyc Corporation
250 Campus Drive
Marlborough, MA 01752
Tel: 508-263-8490
Fax: 508-263-2959

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Application No.	Filing Date	Examiner	Customer No.	Group Art Unit
10/716,704	November 20, 2003	Roy, Anuradha	000038732	3736

Invention: Cytological Evaluation of Breast Duct Epithelial Cells Retrieved by Ductal Lavage

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Attorney's Docket No. 12.017011 DIV

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
Soito *et al.*	Examiner: Anuradha Roy
	Group Art Unit: 3736
Serial No. 10/716,704	
Filed: November 20, 2003	

For: CYTOLOGICAL EVALUATION OF BREAST DUCT EPITHELIAL CELLS RETRIEVED BY DUCTAL LAVAGE

APPEAL BRIEF

Sir:

This Appeal Brief is filed in response to the "Notice of Appeal to the Board of Patent Appeals and Interferences" filed January 6, 2007.

Real Party in Interest.

The real party in interest in this appeal is Cytyc Corporation, Inc., the assignee of the above-referenced patent application.

Related Appeals and Interferences.

There are no related appeals and/or interferences involving this application or its subject matter.

Status of Claims.

Claims 17-23 and 26 are the subject of this appeal. The claims appear in Appendix A. No other claims are pending. Claims 1-16 and 24-25 have been cancelled.

Status of Amendments.

All of Appellants' amendments have been entered.

Summary of Claimed Subject Matter.

This invention relates to a system of cytological evaluation of epithelial cells collected from a human breast duct comprising: a tool or apparatus for accessing a breast duct and collecting breast duct fluid from a human breast while the tool is in the duct; a chart or written guidelines for evaluating the ductal epithelial cells in the sample for one or more observed indicia; and an algorithm for classifying the sample as being normal, atypical or malignant based on the observed indicia. A summary of the claimed subject matter defined in independent claims 17 and 26 involved in the appeal may be found paragraphs [0047] to [0052] of the specification as well as Figures 1 and 2.

Grounds of Rejection to be Reviewed on Appeal.

Whether claims **17-23 and 26** are patentable under 35 U.S.C. § 102(e) over Hung *et al.* (U.S. Patent No. 6,413,228).

ARGUMENT

A. INDEPENDENT CLAIM 17 IS PATENTABLE OVER HUNG *ET AL.*

Claim 17 was rejected under 35 U.S.C. 102(e) as being anticipated by Hung *et al.* (USP No. 6,413,228). In the Office Action dated May 10, 2006, the Examiner argued that Hung *et al.* discloses "...a system of cytological evaluation of epithelial cells (Abstract & Column 28 line 51-Column 29 line 14) collected from a human breast duct comprising:

- A tool (Figure 3) for accessing a breast duct and collecting breast duct fluid from a human breast while the tool is in the duct;
- A chart or written guidelines (Column 13, lines 66-Column 14 line 12) for evaluating the ductal epithelial cells in the sample for one or more observed indicia selected from the group consisting of cell grouping, cell shape, cell size, nuclear size, nuclear shape, presence or absence of nucleoli, nuclear-to-cytoplasmic ratio, vacuoles in the cytoplasm, cytoplasmic shape, cytoplasmic border, presence or absence of anisonucleosis, presence or absence of mitotic figures, nuclear membrane quality, presence of necrotic debris, chromatin distribution, coarseness of chromatin, and the presence or absence of microcalcifications (Column 13, lines 51-55 & Column 25, lines 6-33); and
- An algorithm (Column 12, line 56- Column 17, line 10 & Column 26, lines 35-48) for classifying the sample as being normal, atypical or malignant based upon the observed indicia."

(page 6)

It is the Appellants' position that Hung *et al.* does not anticipate independent claim 17. "[I]nvalidity by anticipation requires that the four corners of a single, prior art document describe every limitation of the claimed invention, either expressly or inherently, such that a person of ordinary skill in the art could practice the invention without undue experimentation." Advanced Display Systems, Inc. v. Kent State University, 212 F.3d 1272 (Fed. Cir. 2000). Hung *et al.* does not meet this standard.

The claimed invention teaches a system of cytological evaluation of epithelial cells collected from a human breast duct comprising: a tool for accessing a breast duct and collecting breast duct fluid from a human breast while the tool is in the duct; a chart or written guidelines for evaluating the ductal epithelial cells in the sample for one or more observed indicia selected from the group consisting of cell grouping, cell shape, cell size, nuclear size, nuclear shape, presence or absence of nucleoli, nuclear-to-cytoplasmic ratio, vacuoles in the cytoplasm, cytoplasmic shape, cytoplasmic border, presence or absence of anisonucleosis, presence or absence of mitotic figures, nuclear membrane quality, presence of necrotic debris, chromatin distribution, coarseness of chromatin, and the presence or absence of microcalcifications; and an algorithm for classifying the sample as being normal, atypical or malignant based on the observed indicia.

The Examiner has not pointed out with clarity and specificity where every limitation of the claimed invention, either expressly or inherently, can be found within the four corners of Hung *et al.* According to the Federal Circuit, anticipation requires the disclosure of "... a single prior art reference of each element of the claim under construction." (W.L. Gore & Assocs. vs. Garlock,

Inc., 721 F.2d 1540, 220 USPQ 303, 313 (Fed. Cir. 1983)). It is not enough that the reference disclose all of the elements in isolation. The Federal Circuit has stated that a prior art reference must disclose each of the elements of a claimed invention "arranged as in the claim". (see Lindemann Maschinenfabrik GmbH vs. American Hoist & Derrick Co., 730 F.2d 1452, 221 USPQ 193 (Fed. Cir. 1984). The prior art reference Hung *et al.* does not disclose each of the elements of the claimed invention arranged as in the present claims.

Independent claim 17 describes a system of cytological evaluation of epithelial cells collected from a human breast duct comprising:

- A tool for accessing a breast duct and collecting breast duct fluid from a human breast while the tool is in the duct;
- A chart or written guidelines for evaluating the ductal epithelial cells in the sample; and
- An algorithm for classifying the sample as being normal, atypical or malignant based upon the observed indicia.

The claimed invention is a system containing a tool for accessing a breast duct; a chart or written guidelines; and an algorithm; together to assist in the cytological evaluation of epithelial cells collected from a human breast duct. In the May 10, 2006 Office Action, the Examiner points to different sections of the specification as support for the argument that Hung *et al.* teaches the system of the present invention. However, the Examiner makes no mention of the reasoning why those particular sections anticipate the claims of the present invention. In the Final Office Action

of October 13, 2006, the Examiner contends that Hung *et al.*'s invention "...does in fact disclose a system containing a tool for accessing a breast duct (Figure 3); a chart or written guidelines (Column 13, lines 51- Column 14, line 12 & Column 25, lines 6-33); and lastly an algorithm (Column 26, lines 35-48); *together* to assist in the cytological evaluation of epithelial cells (Column 12, line 56- Column 13, line 4)." (page 2 of Final Office Action of October 13, 2006). The Appellants respectfully disagree.

A review of the sections of Hung *et al.* cited by the Examiner does not provide every limitation of the claimed invention, either expressly or inherently and, even assuming *arguendo* that all of the claim limitations can be found, each of the elements of the claimed invention are not arranged as in the claim 17.

In the Office Action of May 10, 2006, the Examiner contended that the limitation of "a chart or written guidelines for evaluating the ductal epithelial cells in the sample" was apparently anticipated by Column 13, lines 66-Column 14 line 12 of Hung *et al.* In the Final Office Action of October 13, 2006, the Examiner cited new sections of Hung *et al.* (Column 13, lines 51-Column 14 line 12 & Column 25, lines 6-33) as disclosing the same limitation. The Appellants would argue that aside from being an improper Final Rejection for citing new sections of Hung *et al.*, the sections cited by the Examiner still fail to anticipate the limitation of "a chart or written guidelines for evaluating the ductal epithelial cells in the sample" as recited in claim 17. The sections of Hung *et al.* cited by the Examiner merely list several published methods for <u>studying</u> atypical growth patterns of cells. There is simply no mention of charts or written guidelines for evaluating

the ductal epithelial cells in a sample. In the Final Office Action of October 13, 2006, the Examiner argues that "...given the broadest reasonable interpretation, Examiner contends that Hung *et al.* teaches 'the cells can be studied for atypical growth patterns in individual cells and clusters of cells using *published methods*... (Column 13, line 66-Column 14, line 1),' which anticipates 'written guidelines for evaluating the ductal epithelial cells'." (page 2-3 of the Final Office Action of October 13, 2006). The Appellants disagree that published methods for studying atypical growth patterns in individual cells are equivalent to written guidelines for evaluating ductal epithelial cells. Guidelines are defined as an indication or outline of policy or conduct which are non-subjective by nature. Published methods for the study of growth patterns of cells are merely variable experimental protocols which are used to assist in research. As such, the Appellants would submit that published methods for the study of atypical growth patterns in individual cells and clusters of cells as described in Hung *et al*

. cannot anticipate the limitation of the use of written guidelines for evaluating the ductal epithelial cells as described in claim 17 of the present invention.

Likewise the Examiner rejected claims 17 because the limitation of "an algorithm for classifying the sample as being normal, atypical or malignant based upon the observed indicia" is apparently anticipated by Column 12, line 56- Column 17, line 10 & Column 26, lines 35-48 of Hung *et al.* Column 12, line 56- Column 17, line 10 & Column 26, lines 35-48 of Hung *et al.* is a very large section of the specification listing examples of cellular material, exemplary markers, animal models, and cytological assays. There is simply no mention of an algorithm for classifying

a sample as being normal, atypical or malignant based upon observed indicia. In fact, the word "algorithm" does not appear anywhere in the specification of Hung *et al.* In the Final Office Action of October 13, 2006, the Examiner contends that "...the mere fact that the word 'algorithm' does not appear in Hung *et al*'s specification does not mean an algorithm, defined as a 'set of rules for solving a problem in a finite number of steps,' is not disclosed by Hung *et al.* In fact, Hung *et al.* does disclose as algorithm for classifying the sample as being normal atypical or malignant based upon observed indicia..." (page three of Final Office Action of October 13, 2006). The Examiner then proceeds to cited Hung *et al.* at Column 26, lines 35-48 as an example of an "algorithm" for classifying a sample.

The Appellants respectfully disagree with the Examiner that Hung *et al.* at Column 26, lines 35-48 discloses an algorithm. Even accepting the Examiner's definition of an algorithm as "a set of rules for solving a problem in a finite number of steps", Hung *et al.* still does not teach or suggest an algorithm. Although Hung *et al.* at Column 26, lines 35-48 described how morphology or cellular contents can be used to establish whether or not a cell is normal or cancerous, there is no teaching or suggestion of a set of rules to solve a problem nor is there any mention of a finite number of steps to solve the such a problem. In particular, the Appellants would point out that there is simply no teaching or suggestion of any steps in the section of Hung *et al.* cited by the Examiner. As such, the Appellants would submit that the limitation of "an algorithm for classifying the sample as being normal, atypical or malignant based upon the observed indicia" is not found in Hung *et al.* and therefore Hung *et al.* cannot anticipate claim 17.

Even assuming *arguendo* that Hung *et al.* teaches or suggests all of the elements including a tool, a chart or written guidelines, and an algorithm; there is no suggestion or teaching that all the elements could be combined to make the system of the present invention. As mentioned previously, it is not enough that the reference disclose all of the elements in isolation. The prior art reference must disclose each of the elements of a claimed invention "arranged as in the claim". In Hung *et al.*, there is no teaching or suggestion that each of the elements can be combined into a system for the cytological evaluation of epithelial cells collected from a human breast duct. All of the elements in Hung *et al.* are listed individually with no recognition that they could be combined into a system for cytological evaluation. Since the elements in Hung *et al.* are not arranged as in claim 17, then Hung *et al.* cannot anticipate claim 17.

For all of the reasons stated above, the Appellants respectfully request the withdrawal of the rejection of claim 17 under 35 U.S.C. §102(e).

B. DEPENDENT CLAIMS 18-22 ARE PATENTABLE OVER HUNG *ET AL.*

Dependent claims 18-22 are allowable over the prior art because it is dependent on independent claim 17, and thus contain all the limitations of this independent claim. Appellants respectfully request the withdrawal of the rejection of claims 18-22 under 35 U.S.C. §102(e).

C. DEPENDENT CLAIM 23 IS PATENTABLE OVER HUNG *ET AL.*

The Examiner has rejected dependent claim 23 under 35 U.S.C. § 102(e) as being anticipated by Hung *et al.* (USP No. 6,413,228). In the Office Action dated May 10, 2006, the Examiner argued that Hung *et al.* discloses a system, wherein the algorithm inherently classifies the sample as having insufficient cells to make a diagnosis when the sample has fewer than 10 epithelial cells (Column 33, lines 28-30). There is no mention in Hung *et al.* in of an algorithm for the determination of sample sufficiency if the sample has less than 10 cells. Column 33 lines 28-30 of Hung *et al.* merely define cell clusters as having greater than 10 cells. There is simply no teaching or suggestion in Hung *et al.* of an algorithm capable of determining whether a sample is insufficient if it has less than 10 cells.

For these reasons, Appellants respectfully request the withdrawal of the rejection of claim 23 under 35 U.S.C. §102(e).

D. INDEPENDENT CLAIM 26 IS PATENTABLE OVER HUNG *ET AL.*

Claim 26 was rejected under 35 U.S.C. 102(e) as being anticipated by Hung *et al.* (USP No. 6,413,228). In the Office Action dated May 10, 2006, the Examiner argued that Hung *et al.* discloses "...a system of cytological evaluation of epithelial cells (Abstract & Column 28 line 51-Column 29 line 14) collected from a human breast duct comprising:

- A tool (Figure 3) for accessing a breast duct and collecting breast duct fluid from within the breast duct said tool comprising an elongated portion shaped and sized for extending into the breast duct comprising a single elongated internal lumen through which fluid can be introduced and retrieved from within the breast duct (Column 18, line 24-Column 19 line 15);
- A chart or written guidelines for evaluating the ductal epithelial cells in the sample for one or more observed indicia selected from the group consisting of cell grouping, cell shape, cell size, nuclear size, nuclear shape, presence or absence of nucleoli, nuclear-to-cytoplasmic ratio, vacuoles in the cytoplasm, cytoplasmic shape, cytoplasmic border, presence or absence of anisonucleosis, presence or absence of mitotic figures, nuclear membrane quality, presence of necrotic debris, chromatin distribution, coarseness of chromatin, and the presence or absence of microcalcifications (Column 13, lines 51-55 & Column 25, lines 6-33); and
- An algorithm (Column 12, line 56- Column 17, line 10 & Column 26, lines 35-48) for classifying the sample as being normal, atypical or malignant based upon the observed indicia." (page 6)

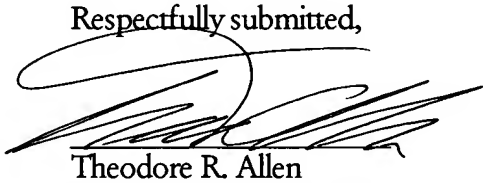
The Examiner makes no further argument as to why Hung *et al.* anticipates claim 26. For the same reasons that Hung *et al.* does not anticipate claim 17, the Appellants would argue that Hung *et al.* does not anticipate claim 26. The Examiner has not pointed out with clarity and specificity where every limitation of the claimed invention, either expressly or inherently, can be found within the four corners of Hung *et al.* The prior art reference Hung *et al.* does not disclose each of the elements of the claimed invention arranged as in the present claims. The sections of Hung *et al.* cited by the Examiner do not provide every limitation of the claimed invention, either expressly or inherently and, even assuming *arguendo* that all of the claim limitations can be found, each of the elements of the claimed invention are not arranged as in the claim 26.

For these reasons, Appellants respectfully request the withdrawal of the rejection of claim 26 under 35 U.S.C. §102(e).

CONCLUSION

In light of the above arguments, the Appellants respectfully submit that the cited reference does not anticipate the claims 17-23 and 26. More specifically, Appellants' claims recite novel features which patentably distinguish over any and all references under 35 U.S.C. §§ 102(e). As a result, a decision by the Board of Patent Appeals and Interferences reversing the Examiner and directing allowance of the pending claims in the subject application is respectfully solicited.

Respectfully submitted,



Customer No, 0000 38732

Theodore R. Allen
Registration No. 41,578
Cytyc Corporation
250 Campus Drive
Marlborough, MA 01752
Tel (508) 263-8490
Fax (508) 263-2959

APPENDIX A: CLAIMS APPENDIX

17. A system of cytological evaluation of epithelial cells collected from a human breast duct comprising: a tool or apparatus for accessing a breast duct and collecting breast duct fluid from a human breast while the tool is in the duct; a chart or written guidelines for evaluating the ductal epithelial cells in the sample for one or more observed indicia selected from the group consisting of cell grouping, cell shape, cell size, nuclear size, nuclear shape, presence or absence of nucleoli, nuclear-to-cytoplasmic ratio, vacuoles in the cytoplasm, cytoplasmic shape, cytoplasmic border, presence or absence of anisonucleosis, presence or absence of mitotic figures, nuclear membrane quality, presence of necrotic debris, chromatin distribution, coarseness of chromatin, and the presence or absence of microcalcifications; and an algorithm for classifying the sample as being normal, atypical or malignant based on the observed indicia.

18. A system as in claim 17, wherein the tool or apparatus for accessing a breast duct comprises a breast duct access and fluid and cell retrieval tool, and one or more of a probe, a tool for administering anesthetic, marking tools for marking an accessed or fluid yielding duct, or a collection receptacle for collecting retrieved fluid and cells.

19. A system as in claim 17, wherein the algorithm classifies the sample as malignant when the sample is characterized by at least an identifying feature selected from the group consisting of a loss of cell cohesiveness, loose clusters of epithelial cells, enlarged cells, enlarged nuclei, high nuclear-to-cytoplasmic ratio, increased cytoplasm in some cells, irregular nuclear membranes, clumped chromatin, hyperchromatic chromatin, unevenly dispersed chromatin, enlarged nucleoli, multiple nucleoli, marked variation among the cells of the sample in cell size and nuclear size, necrotic debris, and microcalcifications in background material appearing as dense material with smooth borders and concentric layers or dystrophic and amorphous.

20. A system as in claim 17, wherein the algorithm classifies the sample as atypical with marked changes when the sample is characterized by at least an identifying feature selected from the group consisting of enlarged ductal epithelial cells, marked nuclear increase in ductal epithelial cells, variation in size and shape of the ductal epithelial cells as compared to normal ductal epithelial cells, abundant cytoplasm in some cells, decreased nuclear-to-cytoplasmic ratios in some cells, coarse chromatin, mild abnormality in chromatin distribution, larger nucleoli than in normal cells, multiple nucleoli, more prominent nucleoli, groups of nuclei that appear to be overlapping, and mitotic figures.

21. A system as in claim 17, wherein the algorithm classifies the sample as atypical with mild changes when the sample is characterized by at least some of an identifying feature selected from the group consisting of single ductal cells, cohesive multilayered cells, complex groups of cells, monolayered cells, an increased number of cell layers compared to normal cells, increased overlapping of the cells, nuclear crowding of cells, minimally enlarged cells, moderate increase in nuclear size to within a range from about 12 to about 16 μm in diameter, slight anisonucleosis in some cells, and presence of nucleoli.

22. A system as in claim 17, wherein the algorithm classifies the sample as normal when the sample is characterized by at least some of an identifying feature selected from the group consisting of single cells, monolayer sheets, tight cells clusters usually one or two cell layers thick, small nuclei in a size range from about 8 to about 12 μm in diameter, high nuclear-to-cytoplasmic ratio depending on the orientation of the cells in clusters, in single cells a columnar shape of cytoplasm, in single cells discreet small vacuoles in the cytoplasm, in single cells discreet cytoplasmic border, cohesive groups of ductal epithelial cells with cells of uniform size and regular round to oval shape, monolayer sheets of cells with uniform, small cells, and monolayer sheets of cells with small inconspicuous nucleoli.

23. A system as in claim 17, wherein the algorithm classifies the sample as insufficient cells to make a diagnosis (ICMD) when the sample has fewer than 10 epithelial cells.

26. A system of cytological evaluation of epithelial cells collected from a human breast duct comprising: a tool for accessing a breast duct and collecting breast duct fluid from within the breast duct said tool comprising an elongated portion shaped and sized for extending into the breast duct comprising a single elongated internal lumen through which fluid can be introduced and retrieved from within the breast duct; a chart or written guidelines for evaluating the ductal epithelial cells in the sample for one or more observed indicia selected from the group consisting of cell grouping, cell shape, cell size, nuclear size, nuclear shape, presence or absence of nucleoli, nuclear-to-cytoplasmic ratio, vacuoles in the cytoplasm, cytoplasmic shape, cytoplasmic border, presence or absence of anisonucleosis, presence or absence of mitotic figures, nuclear membrane quality, presence of necrotic debris, chromatin distribution, coarseness of chromatin, and the presence or absence of microcalcifications; and an algorithm for classifying the sample as being normal, atypical or malignant based on the observed indicia.

APPENDIX B: EVIDENCE

NONE

APPENDIX C: RELATED PROCEEDINGS

NONE